

## REMARKS

Claims 1-19 are pending in the application. Claims 1-11 were rejected. Claims 1-11 have been amended. Claims 12-19 have been added. No new matter has been added. Applicants respectfully request reconsideration of the rejections set forth in the Office Action dated January 30, 2002 in view of the preceding amendments and following remarks.

Claim 1 has been redrafted as a method and recites the limitation that the solution “consists essentially of” the bicarbonate and buffer and optionally “a source of phosphates ions and/or sources of other electrolytes necessary to maintain physiological function and/or an energy source”. Support for these amendments is provided throughout the specification and particularly on page 4, lines 23 to 25, page 5, lines 6 to 9 and page 4, line 20.

Claims 1-11 are rejected under 35 U.S.C. §102(b) as being unpatentable over U.S. Patent No. 4,725,586 to Lindstrom et al. (“Lindstrom”). Applicants respectfully traverse.

Lindstrom discloses a surgical solution for use during surgical procedures for irrigating the eye. The surgical solution of Lindstrom is defined in claim 1 of the patent as follows:

“A composition for irrigating of flushing body tissue during surgical procedures, which composition comprises effective amounts of:

- a. balanced salt solution comprising sodium chloride, potassium chloride, a sodium phosphate buffer system, calcium chloride, and magnesium chloride, the solution having a pH of about 7.4;
- b. chondroitin sulfate;
- c. a buffer system based on N'-2-hydroxyethylpiperazine-N'-ethane sulfonic acid;
- d. 2-mercaptoethanol;
- e. sodium bicarbonate or dextrose;
- f. a pyruvate;
- g. a sodium phosphate buffer system; and,
- h. cystine.”

It is noted that claim 2 of Lindstrom claims a composition according to claim 1 lacking components e, f, g, and h. This results in a composition comprising components a, b, c and d, namely a source of electrolytes in the form of a balanced

salt solution, chondroitin sulfate, HEPES buffer, and 2-mercaptoethanol. This appears to represent the most basic composition of Lindstrom.

The composition of amended claim 1 is limited to the essential features recited in the claim, namely a source of bicarbonate ions, an organic zwitterionic buffer, and optionally sources of phosphate ions and/or electrolytes and/or an energy source. By contrast, the composition of claim 2 of Lindstrom includes, as essential components, a balanced salt solution, chondroitin sulfate, HEPES buffer and 2-mercaptoethanol (see components a, b, c and d of claim 1 above).

As can be seen from the composition of the irrigating solution of the present invention as set out in claim 1 and in Example 1 on pages 6 to 9 of the present application, the irrigating solution of the present application does not contain either chondroitin sulfate or 2-mercaptoethanol, components which are essential to the composition of Lindstrom.

In the surgical solution of Lindstrom, 2-mercaptoethanol is included in the solution to provide a reducing agent:

*“...2-mercaptoethanol is an effective reducing agent that can be utilized by human corneal endothelial cells.”* (column 3, lines 30 to 32 of Lindstrom)

and is necessary for the functioning of the Na<sup>+</sup>-K<sup>+</sup>-ATPase pump of the endothelial cells:

*“...The Na<sup>+</sup>-K<sup>+</sup>-ATPase pump of these endothelial cells requires ATP and reduced pump sites to keep this pump functional. When the pumping action of these corneal epithelial cells is reduced, the cornea imbibes fluids and becomes thickened and loses optical clarity. Therefore, an irrigation solution with a reducing agent is of considerable advantage.”* (column 3, lines 12 to 18 of Lindstrom).

However, the irrigating solution of the present invention does not include 2-mercaptoethanol, yet still functions as an effective irrigating solution and is capable of supporting corneal endothelial function, as demonstrated in Example 1 of the present application, in which the irrigating solution of the present invention demonstrates a similarity in the rate of change of corneal thickness when compared with corneas exposed to BSS Plus.

The chondroitin sulfate which is included in the surgical solution of Lindstrom is a *“highly negatively charged glycosaminoglycan”* (see column 3, lines 40 to 41 of

Lindstrom) and is “*added to replace any glycosaminoglycan that may be removed from the surface of the corneal endothelial cells from the disruption of aqueous flow or surgical trauma*” (see column 3, lines 40 to 44 of Lindstrom). However, the irrigating solution of the present invention is capable of supporting corneal endothelial cell function, despite the absence of chondroitin sulfate as a component of the solution. Once again, the Examiner is referred to Example 1 on pages 6 to 9 of the present application.

Claims 2-10 each depend either directly from independent claim 1 and is therefore respectfully submitted to be patentable over the art of record for at least the reasons set forth above with respect to the independent claim. Further, the dependent claims recite additional elements which when taken in the context of the claimed invention further patentably distinguish the art of record.

For at least these reasons, Lindstrom does not teach a method as recited in claims 1-10; and withdrawal of the rejection under 35 U.S.C. § 102(b) is respectfully requested.

Although the Examiner has not specifically raised an obviousness rejection, it is believed that the amended claims are non-obvious over the cited prior art as the composition of the present invention provides a simple effective medium for use in ocular irrigation during surgery (as shown by the examples). Such a composition cannot be derived from Lindstrom, which teaches the essential presence of chondroitin sulphate and 2-mercaptoethanol, neither of which are required in the composition of the present invention. In particular, there is nothing in Lindstrom, nor any other prior art of record, which suggests that essential elements of the composition of Lindstrom could be omitted and an effective ocular irrigating solution obtained. As a result, we consider that the claimed composition is patentable.

Thus, in summary, Applicants respectfully submit that the amended claims presented herewith represent subject-matter which is both novel and non-obvious over the Lindstrom reference.

New composition of matter as recited in amended claim 11 and new claims 12 to 19 have been added and are directed to a narrower definition of the irrigating

solution to that defined in amended method claim 1. The subject-matter of these claims is also patentable over the disclosure of Lindstrom for at least the reasons already mentioned above with respect to the novelty of method claim 1. In addition, compared with amended method claim 1, Claims 11 to 19 further specify that the bicarbonate source is present in the irrigating solution at a concentration of from 10 to 50 mmol/l and also require the presence of sources of electrolytes to maintain physiological function.

Conclusion

In view of the foregoing, Applicant believes that all pending claims are allowable and respectfully requests a Notice of Allowance from the Examiner. Should the Examiner believe that a telephone conference would expedite the prosecution of this application, the undersigned can be reached at the number set out below. If any fees are due in connection with the filing of this paper, the Commissioner is authorized to charge such fees to Deposit Account 50-0388 (Order No. HASLP004).

Respectfully submitted,  
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Limited Recognition under 37 C.F.R. §10.9(b)

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## APPENDIX TO SHOW CHANGES MADE

### **In the Claims:**

1. (Once Amended) [An ocular irrigating solution for irrigating the eye during surgery comprising, a source of bicarbonate ions and] A method of irrigating the eye of a patient during surgery comprising supplying to the eye a solution consisting essentially of a source of bicarbonate ions, a physiologically acceptable organic buffer which is an organic zwitterionic buffer having a buffering capacity within the range pH 6.8 to 8.0, and optionally a source of phosphate ions and/or source of electrolytes necessary to maintain physiological function and/or an energy source.
2. (Once Amended) [An ocular irrigating solution] A method according to claim 1, wherein the organic buffer maintains the solution at a pH in the range 7.2 to 7.8.
3. (Twice Amended) [An ocular irrigating solution] A method according to claim 1, wherein the organic buffer is a zwitterionic amino acid.
4. (Once Amended) [An ocular irrigating solution] A method according to claim 3, wherein the organic buffer is N-2-(hydroxyethyl) piperazine-N'-(2-ethanesulfonic acid).
5. (Twice Amended) [An ocular irrigating solution] A method according to claim 1, wherein the concentration of the buffer is from 10 to 50 mmol/l.
6. (Twice Amended) [An ocular irrigating solution] A method according to claim 1, wherein the bicarbonate source is sodium bicarbonate.
7. (Once Amended) [An ocular irrigating solution] A method according to claim 6, wherein the bicarbonate source is preferably present in the solution to give a bicarbonate concentration of about 10 to 50 mmol/l.
8. (Twice Amended) [A ocular irrigating solution] A method according to claim 1 [which] wherein the solution does not contain glucose, or any other energy source which tends to degrade at physiological pH over extended time periods.
9. (Twice Amended) [A ocular irrigating solution] A method according to claim 1 wherein the solution has [having] been sterilized by an autoclaving procedure.
10. (Once Amended) [An ocular irrigating solution according to claim 1, for use in a surgical method performed on the eye] A method according to claim 1 wherein the ocular irrigating solution claim 1 replaces fluid loss during surgery and maintains corneal function.
11. (Twice Amended) [A method of surgery performed on the human eye in which an ocular irrigating solution according to claim 1 is employed to replace fluid loss during the operation and to maintain corneal function ] An ocular irrigating solution for irrigating the eye during surgery consisting essentially of a source of bicarbonate ions, a physiologically acceptable organic buffer which is an organic zwitterionic buffer having a buffering capacity within the range pH 6.8 to 8.0, sources of electrolytes

necessary to maintain physiological function and optionally a source of phosphate ions and/or an energy source, and wherein the bicarbonate source is present in the solution to give a bicarbonate concentration of from 10 to 50 mmol/l.

12. (Once Amended) [An ocular irrigating solution substantially as hereinbefore described, with reference to the accompanying examples] An ocular irrigating solution according to claim 11 wherein the organic buffer maintains the solution at a pH in the range 7.2 to 7.8.

13. (New) An ocular irrigating solution according to claim 11 wherein the organic buffer is a zwitterionic amino acid.

14. (New) An ocular irrigating solution according to claim 11 wherein the organic buffer is N-2- (hydroxyethyl) piperazine-N'- (2- ethanesulfonic acid).

15. (New) An ocular irrigating solution according to claim 11 wherein the concentration of the buffer is from 10 to 50 mmol/l.

16. (New) An ocular irrigating solution according to claim 11 wherein the bicarbonate source is sodium bicarbonate.

17. (New) An ocular irrigating solution according to claim 11 wherein the bicarbonate source is present in the solution to give a bicarbonate concentration of from 15 to 25 mmol/l.

18. (New) An ocular irrigating solution according to claim 11 which does not contain glucose, or any other energy source which tends to degrade at physiological pH over extended time periods.

19. (New) An ocular irrigating solution according to claim 11 having been sterilized by an autoclaving procedure.